REMARKS

Claims 1-3, 6, 13, and 14 are pending in the application.

Claim Rejections -- 35 U.S.C. § 112

There is a single remaining rejection in this case. Claims 1-3, 6, 13 and 14 stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the claims are not enabled on the ground that "[g]iven the unpredictability in the art of therapeutic transplantation, the development of therapeutic protocols requires substantial experimentation. In view of the limited guidance, this substantial experimentation rises to the level of undue experimentation." (Office Action at page 4). Applicant traverses. The Examiner has provided no evidence to support this assertion. The standard for enablement does not require human clinical trials. Nonetheless, Applicant notes that the neurospheres recited in the claimed methods are presently involved in Phase I human clinical trials for the treatment of lysosomal storage disorders (a summary of this study is provided as Exhibit 1, which is available at http://clinicaltrials.gov/ct/show/NCT00337636?order=1). This clinical trial is evidence that the methods of the instant invention are enabled. The following passage from the MPEP is instructive:

> Before a drug can enter human clinical trials, the sponsor, often the applicant, must provide a convincing rationale to those especially skilled in the art (e.g., the Food and Drug Administration) that the investigation may be successful. Such a rationale would provide a basis for the sponsor's expectation that the investigation may be successful. In order to determine a protocol for phase I testing, the first phase of clinical investigation, some credible rationale of how the drug might be effective or could be effective would be necessary. Thus, as a general rule, if an applicant has initiated human clinical trials for a therapeutic product or process, Office personnel should presume that the applicant has established that the subject matter of that trial is reasonably predictive of having the asserted therapeutic utility.

MPEP § 2107.03 (IV) Human Clinical Data (emphasis in original).

Furthermore, the specification and Examples teach those of ordinary skill in the art how to use the claimed methods without undue experimentation. One of ordinary skill in the art would be able to routinely use the methods described in the application. The specification is replete with support for the claimed methods. *See, e.g.*, Specification at pages 14-16; page 31, line 23 through page 32, line 3; page 35, line 24 through page 36 line 2; page 37, lines 1-9; and page 41, lines 11-12 and particularly Example 15. Moreover, the specification also contains

working examples (*see, e.g.* Examples 8, 9, and 15) which illustrate that the claimed methods do not require undue experimentation. Transplantation using the claimed methods has been shown to increase graft survival, promote reinnervation of host tissue (as well as the associated behavioral recovery), and enhance the effectiveness of neural stem cell transplantation as a restorative therapy for treating neurodegenerative diseases. *See, e.g.*, Specification at page 41, lines 12-17.

In short, there is ample evidence of record that demonstrates how to transplant neural stem cells into the brain of a living host subject, thereby increasing graft survival and enhancing the effectiveness of the transplantation, while also maintaining the cells' ability to subsequently differentiate into neurons, oligodendrocytes, or astrocytes. (*See, e.g.*, Specification at page 6, line 24 through page 7, line 7; page 15, line 22; page 15, line 26 through page 16; line 16; and Examples 9 and 15.) In view of the arguments presented above, Applicant submits that the claims are fully enabled by the as-filed specification. The rejection under 35 U.S.C. § 112, first paragraph should be withdrawn.

CONCLUSION

Applicant submits that this paper is fully responsive and that the application is in condition for allowance. Such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Dated: February 7, 2007

Ivor R. Elrifi, Reg. No. 39,529
Christina K. Stock, Reg. No. 45,899
Attorneys for Applicant
Telephone: (617) 542-6000
Facsimile: (617) 542-2241
Customer Number **30623**.

Enclosures: Exhibit 1

Study of the Safety and Preliminary Effectiveness of Human Central Nervous System (CNS) Stem Cells (HuCNS-SC) in Patients With Infantile or Late Infantile Neuronal Ceroid Lipofuscinosis (NCL)

This study is currently recruiting patients.
Verified by StemCells, Inc. September 2006

Sponsored by: StemCells, Inc.
Information provided by: StemCells, Inc.
ClinicalTrials.gov Identifier: NCT00337636

Purpose

Patients with infantile or late infantile NCL have either a reduced amount of, or are missing, the palmitoyl protein thioesterase 1 (PPT1) enzyme or the tripeptidyl peptidase 1 (TPP-I) enzyme. Human central nervous system stem cells (HuCNS-SC) are an investigational product derived from human brain cells. HuCNS-SC have been shown to survive and migrate within the brains of mice. When grown in the laboratory, HuCNS-SC have been shown to produce the PPT1 and TPP-I enzymes. In mice missing the PPT1 enzyme, HuCNS-SC have been shown to increase the amount of this enzyme in the brain, to reduce the amount of abnormal storage material in the brain, and to prevent the death of some neurons (a type of cell) in the brain.

Participation in this study will involve screening assessments, surgery to implant HuCNS-SC, medication to suppress the immune system, and a series of follow-up assessments. The length of time from the start of screening through to the last follow-up visit will be approximately 13 months, with frequent visits to the study center during this time. After completion of this study, patients will be monitored for an additional 4 years under a separate long term follow-up protocol.

Condition	Intervention	Phase
Neuronal Ceroid Lipofuscinosis	Procedure: Surgery to implant human CNS stem cells (HuCNS-SC) Drug: Medication to suppress the immune system	Phase I

MedlinePlus related topics: Degenerative Nerve Diseases; Genetic Disorders; Metabolic Disorders
Genetics Home Reference related topics: Degenerative Nerve Diseases; Metabolic Disorders

Study Type: Interventional
Study Design: Treatment, Non-Randomized, Open Label, Dose Comparison, Single Group Assignment, Safety/Efficacy Study

Official Title: A Phase I Study of the Safety and Preliminary Effectiveness of Human CNS Stem Cells (HuCNS-SC) in Patients With Neuronal Ceroid Lipofuscinosis Caused by Palmitoyl Protein

Thioesterase 1 (PPT1) or Tripeptidyl Peptidase 1 (TPP-I) Deficiency

Further study details as provided by StemCells, Inc.:

Expected Total Enrollment: 6

Study start: May 2006

Eligibility

Ages Eligible for Study: 1 Year - 12 Years, Genders Eligible for Study: Both

Criteria

Inclusion Criteria:

Patients MAY be eligible to participate in this research study if they:

- Are age 1 to 12 years old
- Have a clinical diagnosis of infantile neuronal ceroid lipofuscinosis (INCL) or late infantile neuronal ceroid lipofuscinosis (LINCL)
- Have a mutation of the CLN1 or CLN2 gene
- Have severe cognitive, communication, behavior and language impairment

Exclusion Criteria:

Patients may not be eligible to participate in this research study if they:

- Have cognitive, communication, behavior and language function less than that of a 1 year old
- Have previously received an organ, tissue or bone marrow transplantation
- Have previously participated in any gene or cell therapy study
- Have infection with hepatitis virus, Cytomegalovirus, Epstein Barr Virus, or Human Immunodeficiency Virus (HIV)
- Have a current or prior cancer
- Have a bleeding disorder
- Are unable to have an MRI scan

Location and Contact Information

Please refer to this study by ClinicalTrials.gov identifier NCT00337636

Jennifer Penfield, MS, PA-C 503 494-7944 Penfield@OHSU.edu

Oregon

Oregon Health and Science University, Portland, Oregon, 97239, United States; Recruiting
Robert Steiner, MD, Principal Investigator

Study chairs or principal investigators

Robert Steiner, MD, Principal Investigator, Oregon Health and Science University

More Information

Click here for information about StemCells, Inc.

Study ID Numbers: CL-N001-05
Last Updated: September 27, 2006
Record first received: June 13, 2006
ClinicalTrials.gov Identifier: NCT00337636
Health Authority: United States: Food and Drug Administration
ClinicalTrials.gov processed this record on 2007-02-06